

REMARKS

This is a full and timely response to the Office Action mailed January 25, 2008, submitted concurrently with a Request for Continued Examination and a two month extension of time to extend the due date for response to June 25, 2008.

By this Amendment, claims 1, 7, 9 and 10 have been amended to more particularly define the present invention and to overcome the rejection under 35 U.S.C. §112, second paragraph. Thus, claims 1-11 are currently pending in this application. Support for the claim amendments can be readily found variously throughout the specification and the original claims, see, in particular, pages 7-9 of the present specification.

In view of these amendments, Applicant believes that all pending claims are in condition for allowance. Reexamination and reconsideration in light of the above amendments and the following remarks is respectfully requested.

Rejection under 35 U.S.C. §112

Claims 1-11 are rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite. Applicant believes that the amendments to claim 1 overcome this rejection by the deleting the term “*derivative*” from the claims. Thus, withdrawal of the present rejection is respectfully requested

Rejections under 35 U.S.C. §102 and §103

Claims 1-4 and 8-11 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Bauer et al., (2000. Rapid Comm. In Mass Spectrometry. Volume 14, Issue 10, Pages 924-929). Further, claims 1-4 and 9-11 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Keough et al., (Proc. Natl. Acad. Sci., Vol. 96, pp. 7131-7136, June 1999). Lastly, claims 1-11 are rejected under 35 U.S.C. §103(a) as allegedly being obvious over Turecek (J. Mass Spectrometry. 2002; 37: 1-14) in view of Keough et al. Applicant respectfully traverses these rejections.

To constitute anticipation of the claimed invention under U.S. practice, the prior art reference must literally or inherently teach each and every limitation of the claims. Further, to establish a *prima facie* case of obviousness, the cited reference(s) must teach or suggest the

invention as a whole, including all the limitations of the claims. Here, in this case, none of the cited references, either alone or in combination, teach or suggest all of the limitations of the claims with particular emphasis on the limitations “*preparing an amino acid, wherein said amino acid (a) is obtained from any of α -amino acid, β -amino acid, γ -amino acid, and δ -amino acid, (b) is negatively charged as a whole molecule, (c) comprises a side chain containing an acidic group, and (d) comprises an amino group protected with a protective group which (i) prevents the amino group from becoming positively charged and (ii) maintains the negative charge of the molecule as a whole in water*”.

More specifically, the claims have been amended to more particularly define the features of the protective group (“*wherein the protective group prevents the amino group of the amino acid from becoming positively charged and maintains the negative charge of the molecule as a whole in water*”) and the acidic group in the side chain (“*dissociation of the proton from the acidic group so that the amino acid becomes negatively charged*”) in attaining the important characteristics of the claimed amino acid (“*negatively charged as a whole molecule*”) and the required effect of the present invention (i.e. “*reacting the negatively charged amino acid to the N-terminus of the peptides or the peptide fragments facilitates the generation of the positively charged product ions*”) for determining the amino acid sequence of a peptide. Applicant strongly believes that such features and characteristics are not present or disclosed in Bauer et al. Keough et al. and Turecek.

In the present invention, the protective group serves to prevent the amino group of the amino acid from becoming positively charged and thereby, when the peptide of interest is reacted with the amino acid and subjected to mass spectrometry, facilitate the generation of positively charged product ions that are not bound to the amino acid (see page 9 of the specification). If the amino acid is not protected with the protective group, the positive charge on the amino group of the amino acid may cancel out with the negative charge of the side chain (which occurs due to the proton dissociation from the acidic group), thus interfering with the generation of such positively charged product ions as described above.

As an example of the claimed amino acid, the particularly preferred amino acid, N-biotinylcysteic acid of chemical formula (I), becomes a negatively charge molecule in water and this negative charge is not lost due to the presence of the biotinyl group as the protective group.

In contrast to the present invention, Bauer et al. discloses the peptide-derivatizing method in which *“the sulfonic acid derivatization of the N-terminus using chlorosulfonylacetyl chloride and performic acid oxidation of cysteine”* (see page 925, left column, ‘*N-Terminal derivatization*’ paragraph, of Bauer et al.). Namely, Bauer et al. discloses reacting peptide with a component which is not an amino acid (i.e. the component being chlorosulfonylacetyl chloride). Thus, Bauer et al. never discloses reacting a peptide with an amino acid which has the specifically claimed structure of (a) *being obtained from any of α -amino acid, β -amino acid, γ -amino acid and δ -amino acid*, (b) *being negatively charged as a whole molecule*, (c) *comprising a side chain containing an acidic group*, and (d) *comprising an amino group protected with a protective group which (i) prevents the amino group from becoming positively charged and (ii) maintains the negative charge of the molecule as a whole in water*.

Likewise, Keough et al. also discloses reacting a peptide with a component which is not an amino acid. Keough et al. discloses the peptide-derivatizing method in which the *“coupling of either 2-sulfobenzoic acid cyclic anhydride or chlorosulfonylacetyl chloride to the N-terminus of peptides”* (see page 7132, ‘*N-terminal Derivatization Procedures*’ paragraph, of Keough et al.) is involved; *“N-terminal sulfur that subsequently could be oxidized”* (see page 7133, right column, lines 5-15, of Keough et al.); and *“Sulfobenzoic acid cyclic anhydride (V) couples readily to free amines in aqueous solution”* (see page 7133, right column, lines 17-22, of Keough et al.). Hence, it is clear that Keough et al. discloses reacting a peptide with a component which is not an amino acid (i.e. the component being 2-sulfobenzoic acid cyclic anhydride or chlorosulfonylacetyl chloride). Thus, like Bauer et al., Keough et al. never discloses reacting a peptide with an amino acid which has the specific structures as recited in amended claim 1 noted above.

This deficiency in Bauer et al. and Keough et al. is not cured by the teachings and suggestion of Turecek. Turecek does not teach a method involving the addition of an amino acid, as the Examiner mentioned on page 11, lines 13 and 14, of the Office Action.


Thus, since none of the cited references teach or suggest reacting a peptide with an amino acid having the specific structures recited in amended claim 1 noted above, Applicant believes that the present invention would not be anticipated by and render obvious over the cited references. Hence, for these reasons, withdrawal of the present rejections is respectfully requested.

CONCLUSION

For the foregoing reasons, all the claims now pending in the present application are believed to be clearly patentable over the outstanding rejections. Accordingly, favorable reconsideration of the claims in light of the above remarks is courteously solicited. If the Examiner has any comments or suggestions that could place this application in even better form, the Examiner is requested to telephone the undersigned attorney at the below-listed number.

Dated: June 25, 2008

Respectfully submitted,

By:  _____

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